Appendix F

SENSITIVITY ANALYSES OF KEY UNCERTAINTIES IN THE RISK ASSESSMENT

As indicated in Chapter VI, a number of assumptions are involved in conducting a quantitative risk analysis of the effects of ambient PM, and any such effort involves a number of significant uncertainties. Sensitivity analyses are one approach that can provide insight into the potential effects of uncertainties and selection of alternative input assumptions on the risk analyses results. The results of a number of sensitivity analyses for the risk analyses are presented below. A more detailed discussion of the sensitivity analyses conducted for the PM health risk assessment can be found in the technical support document (Abt Associates, 1996b).

A. Sensitivity Analyses of Key Air Quality Uncertainties

1. Sensitivity Analysis of Alternative Background Concentrations

An important uncertainty concerning the air quality information used in the risk analysis involves estimates of background concentrations (see Table IV-3 for range of estimated background PM_{10} and $PM_{2.5}$ concentrations based on Chapter 4 of the CD). For the base case PM risk estimates, effects were quantified across the range of observations in the original study or to background concentrations, whichever was higher. For the base case risk analysis results reported in Chapter VI, the midpoint of the range of estimated annual background concentrations has been used. Tables F-1A and F-1B show the sensitivity of the risk estimates to using either the low end of the annual background concentration range identified in the CD (5 $\mu g/m^3$ PM_{10} and 2 $\mu g/m^3$ $PM_{2.5}$ in the eastern U.S.) or the high end of the annual background concentration range identified in the CD (11 $\mu g/m^3$ PM_{10} and 5 $\mu g/m^3$ $PM_{2.5}$ in the eastern U.S.) as the estimate for background concentrations rather than the midpoint of the range.

One important point from Table F-1A and F-1B is that the estimates of mortality and bronchitis risks associated with long-term exposure to PM do not change as a result of alternative background concentrations. Because these long-term studies relate health effects to annual mean concentrations, and the lowest observed annual mean concentration (the limit used for quantification of risk) is well in excess of current estimates of background (e.g., the range of concentrations observed for the cities in the ACS study (Pope et al., 1995) was 9.0 - 33.4 $\mu g/m^3$

$PM_{2.5}$), the estimates of health risks associated with these endpoints do not change in relation to estimates of background concentrations in the ranges used here (e.g., 2 -5 µg/m^3 $PM_{2.5}$).

2. Sensitivity of Health Risks Estimates to Alternative Rollback Methods for Simulating Attainment of Alternative Standards

In addition to uncertainties concerning "as is" air quality, there is inherent uncertainty concerning any effort to estimate air quality distributions that would occur upon attaining standards at some future date. In the risk analysis, such uncertainties are introduced both in efforts to model health risks upon attainment of the current standard (Chapter VI, Table VI-8) and upon attainment of alternative $PM_{2.5}$ standards (Chapter VI, Tables VI-12a -13b). The base case analysis assumes that proportional reductions would be observed in air quality concentrations as an area attained either a controlling annual mean or 24-hr standard. A sensitivity analysis was conducted to examine the sensitivity of risk reduction estimates associated with alternative $PM_{2.5}$ standards to an alternative assumption concerning the pattern of air quality rollbacks and the resulting air quality distribution that might be observed in reaching attainment of $PM_{2.5}$ standards (Table F-2). Because $PM_{2.5}$ standards do not currently exist, information on past air quality rollbacks in response to $PM_{2.5}$ standards is not available. However, monitoring information for $PM_{2.5}$ can be examined, although it is uncertain how much of the variation observed between years in the air quality distribution at a location reflects actual control strategies versus more general year-to-year variability. In a preliminary examination of changes in the distribution of $PM_{2.5}$ concentrations from sites with multiple years of data (from AIRS and CARB data sets), Abt Associates found that proportional rollback reasonably approximated the central tendency of variations in $PM_{2.5}$ air quality distributions, however, considerable variation could be observed in this relationship across time and location (see Abt Associates, 1996b for more information).

An attempt to bound the potential effects of alternative PM air quality reduction patterns has been examined in a sensitivity analysis of PM-associated risks by choosing alternative assumptions for modeling $PM_{2.5}$ rollbacks. Table F-2 shows the sensitivity of risks reduction estimates associated with alternative $PM_{2.5}$ standards to the rollback assumption in which the upper 10% of the $PM_{2.5}$ 24-hr air quality concentrations are reduced by a larger amount (a ratio of 1.6) than in the remaining 90% of the distribution of PM air quality concentrations. This alternative rollback case is intended to model a control strategy that preferentially targets peak $PM_{2.5}$ levels. The proportion of preferential reduction in peak concentrations (a 1.6 ratio in reduction for the upper 10% of concentrations) is based on empirical observation of the 99th percentile of observed year-to-year variation in $PM_{2.5}$ air quality among site-years for all available $PM_{2.5}$ monitoring sites with multiyear data from the AIRS or CARB $PM_{2.5}$ datasets.

Table F-2 shows for both a proportional rollback and the preferential peak reduction rollback the amount of reduction in $PM_{2.5}$ concentrations necessary to reach alternative standards (for simplicity, the annual and daily standards are considered alone) and the air quality distribution (summarized as the annual mean and 2nd daily max concentration) that is projected to occur upon attainment. In this example, the annual standard provides less of a change in total incidence of health effects, but this is simply a consequence of the annual standard chosen (15 $\mu g/m^3$) being less controlling than the daily standard chosen (50 $\mu g/m^3$) for Philadelphia County (Chapter VI, Table 11b).

More important to consider are the PM-associated risk reductions and resulting air quality observed when the operation of the same standard (annual or daily) is modeled under the two rollback cases rather than any comparison of total incidence reduction between the two standards. The important observation is that estimated changes in incidence of health effects provided by attainment of annual standards are less sensitive to deviation from the base case assumption on rollback than estimated reductions in health effects incidence risk resulting from attainment of a daily standard. For instance, the results in Table F-2 indicate that for a controlling annual standard, past patterns of air quality change would suggest the reduction in health effects from short-term exposures, as represented by mortality from short-term exposures, could potentially vary more than 35% with a controlling 24-hr standard (mean change in total incidence of 70 versus 110), compared to approximately 25% with a controlling annual standard. For mortality from long-term exposures, this contrast is greater. For example, under a controlling short-term standard estimated risk reduction could potentially vary 30%, while under an annual standard there would be no change in estimated risk reduction. This is a result of the fact that mortality from long-term exposures are related to central estimate air quality measures such as annual mean concentration in the reported concentration-response relationships, thus the distribution of 24-hr concentrations associated with this annual mean concentration does not influence the estimated health risk reduction as long as the same annual mean (in this case, 15 $\mu g/m^3$) is achieved under both rollback conditions.

Figure F-1 illustrates some of the characteristics of the integration of current air quality distributions and reported concentration-response relationships as used to predict the total risk from ambient particle exposures across a year. Figure F-1 shows the relative contribution of different portions of the ambient $PM_{2.5}$ concentration distribution for Philadelphia County to the "as is" mortality health risk from short-term exposures. The Figure shows in bar graph form the proportion of total observed PM-2.5 concentrations across the year (in groups of 4 $\mu g/m^3$ per bar), with the number of days out of the whole year (361 observations) that concentrations fell within each concentration range shown on the left-hand Y axis. On top of this frequency distribution has been overlaid the proportion of "as is" mortality risk under base case assumptions associated with each 4 $\mu g/m^3$ concentration range (Since "as is" mortality risk from short-term exposures was calculated using a two-day mean averaging time, the averaging time used at the largest number of mortality study locations, the proportion of "as is" mortality risk is calculated for each two-day mean interval of 4 $\mu g/m^3$). This Figure shows that for base case assumptions, concentrations in the range of 16-20 $\mu g/m^3$ contribute the largest amount to the estimated mortality risk on an annualized basis for Philadelphia County. Even though concentrations in the range of 44 $\mu g/m^3$ $PM_{2.5}$ and above clearly contribute more mortality per day for these concentrations, the much larger number of days within the 16-20 $\mu g/m^3$ range results in this interval being associated with the largest total risk. Standards with

Figure F-1. Distribution of $PM_{2.5}$ Concentrations and of Estimated Mortality Risks from Short-Term Exposures in Philadelphia County

a 24-hr averaging time are traditionally based on peak air quality statistics, concentrations for which the risk on an individual day is highest, but, as a result of the ambient air quality distribution and the $PM_{2.5}$ concentration-response functions that have been observed, appear to contribute a relatively small amount of the total health risk compared to the distribution as a whole. The annual mean statistic contains information about the aggregate total of all the air quality concentrations, a quantity similar to the quantity of all air quality concentrations minus estimated background that contributes to estimates of annualized mortality risk in the base case risk analysis.

The difference between the air quality distribution as a whole and that estimated to contribute to aggregate annualized health risk will be more pronounced if assumptions about a substantial cutpoint concentration are made. However, even in these cases, the aggregate annualized risk will be a function of the concentrations across a wide portion of the upper end of the $PM_{2.5}$ air quality distribution. Since reducing high concentration days can provide a greater microgram reduction in $PM_{2.5}$ annual average mass for a lesser percentage reduction in air quality, an annual standard will still favor reducing high concentration values. In contrast to the 24-hr standard, however, an annual standard is less likely to allow areas whose air quality concentrations are substantially above those necessary for attainment to reduce concentrations in a fashion that might not result in meaningful risk reduction (e.g., by reducing just a few high peak values). In so doing, an annual controlling standard might be expected to lead to less variation in the risk reduced in different geographic areas having similar initial air quality that reduce PM concentrations to attain a set of $PM_{2.5}$ alternative standards.

Table F-2 conveys this point in a related fashion. Table F-2 shows that under the preferential peak reduction rollback considered, the lower 90% of air quality concentrations are reduced only 18% versus the 30% reduction observed if the entire distribution is reduced evenly. Because the lower 90 percent of the air quality values contribute so substantially to the aggregate annualized risk (Figure F-1), a lesser reduction across this wide range of concentration values leads to less total $PM_{2.5}$ reduction [as reflected by the higher annual mean upon attainment of a daily standard of 50 $\mu g/m^3$ in which lower concentrations have been less substantially reduced

(13.6 $\mu g/m^3$) than when concentrations have been reduced evenly (12.6 $\mu g/m^3$)], and thus less total annual health risk being reduced.

Absent information that allows the possibility to be excluded that PM concentrations through a wide portion of the air quality distribution may contribute to risk, an annual controlling standard is likely to be less sensitive to alternative rollback assumptions. This is in large part because the standard employs an air quality measure (the annual mean) that inherently captures more information reflective of the concentrations across the bulk of the air quality distribution. In general, annual standards would be expected to decrease uncertainty in risk reductions observed for areas that might undergo different air quality rollbacks to reach attainment of $PM_{2.5}$ alternative standards relative to comparably stringent controlling 24-hr standards.

For the special case of modeling the "attainment of current PM_{10} standards" case for Los Angeles County, since the current daily PM_{10} standard is controlling in Los Angeles, it is relevant to consider the potential effects of variations from a proportional rollback for PM_{10} on the risk estimates for alternative $PM_{2.5}$ standards. Variations in the PM_{10} rollback that would result in attainment of the current standards from the proportional rollback assumed could either increase or decrease the amount of risk associated with PM remaining to be affected by alternative $PM_{2.5}$ standards. In addition, the risk estimate for the "attainment of the current standards" case in Los Angeles has an important additional source of uncertainty relating to patterns of reductions. If control strategies to meet the current PM_{10} standards preferentially reduce the coarse fraction of PM_{10} in relation to the fine fraction of PM_{10}, risks associated with $PM_{2.5}$ as an indicator of PM under the "attain current standards" case could be higher and, thus, proportions of estimated risk reduced under the alternative $PM_{2.5}$ standards also would be greater. Alternatively, if control strategies to meet the current standards preferentially reduce the fine fraction, then risks associated with $PM_{2.5}$ as an indicator of PM would be less under the "attain current standards" and the proportion of estimated risks reduced under the alternative $PM_{2.5}$ standards would be less.

B. Sensitivity Analyses of Key Concentration-Response Uncertainties

The area of the risk analysis with the largest number of uncertainties amenable to sensitivity analyses involves the application of PM concentration-response relationships in the risk analysis. The sensitivity of risk estimates for "as is" air quality in Philadelphia has been analyzed to determine the potential impact of alternative analytic approaches to addressing uncertainty in the concentration-response relationships. The following sensitivity analyses about concentration-response relationships are summarized in this Section:

- The effect of alternative assumptions concerning the shape of the concentration-response relationships, especially concerning the effect of cutpoint concentrations below which variations in PM concentration are not associated with increases in risk, is analyzed. Alternative assumptions about the slope of the concentration-response relationship above any presumed cutpoints also is addressed.

- The effect of pooling studies to combine information from a number of studies to apply to the two risk analysis locations is examined. The sensitivity of short-term mortality risk estimates is analyzed, especially with respect to the effects of combining studies that are heterogenous in averaging time.

- The effect of using coefficients for PM obtained simultaneously with other copollutants in the regression model is addressed.

- The effect of alternative assumptions concerning the potential role of air quality previous to that monitored in studies of the effects on mortality associated with long-term exposure is examined.

All of these sensitivity analyses are conducted using "as-is" air quality in Philadelphia County. Further sensitivity analyses are provided in the technical support document (Abt Associates, 1996b).

1. Sensitivity Analyses of Alternative Cutpoint Concentrations

Tables F-3A-E present the results from sensitivity analyses of different alternative cutpoint concentrations for short-term and long-term exposures to PM. The concentrations chosen as cutpoints for these sensitivity analyses were selected from the analysis of potential cutpoints of interest described in Appendix E and summarized in Chapter VI. For the base case analysis, no cutpoint has been assumed. In the sensitivity analyses, various cutpoint concentrations have been examined, and no health risks associated with PM are estimated for any days whose 24-hr concentrations are below the specified cutpoint concentration. In addition, the slope of the relationship above the cutpoint has been remodeled using one of two approaches. For both approaches, the relationship is assumed to begin at zero increased risk at the cutpoint concentration, and to extend upward with an increased slope compared to the original reported relationship (see Fig. VI-6). In Approach 1 it is assumed that the new slope would increase to an extent where the increased health risk predicted at the highest concentration is increased proportional to the proportion of the range of original concentrations that fall below the cutpoint. While this adjustment produces a slope resembling those generally posited to result in a model incorporating a cutpoint (e.g., Fig VI-6), there is no clear guidance on how to most appropriately model changes in slope for purposes such as the PM risk analysis (where, for instance, primary datasets are not readily available).

In light of this uncertainty, a second approach, involving a more minimal adjustment to slope (labeled "Approach 2" on Figure VI-6) also has been carried out as a potential lower bound for an adjusted slope. In Approach 2, the concentration-response relationship has been remodeled to begin at zero at the cutpoint and intersect with the same health risk estimated at the highest concentrations observed in the original relationship. As cutpoints are chosen that exclude successively larger number of observations, it is expected that the milder degree of increased slope represented by Approach 2 would be less likely to be observed.

Figure F-2 suggests that relatively mild increases in slope may be observed for some TSP concentration-response relationships compared to a linear model meta analysis from the CD. However, other TSP concentration-response relationships which examined cutpoints well within the range of data observed a pattern of increased slope more like that modelled in Approach 1 (Philadelphia 1983-88, which included SO_2 and O_3 in the analysis, compared with a meta analysis of PM coefficients from models including copollutants).

As might be expected, Tables F-3A - D indicate that the two slope adjustment approaches agree mostly closely at the lowest cutpoint concentration. In addition, these tables suggest that the method of adjusting the slope of the remaining relationship is less important to the estimates of health risk than the choice of cutpoint concentration itself. The higher the cutpoint, the greater the proportion of observations for each city that is associated with no increase in risk. Depending on judgments concerning the weight to be given the estimates at

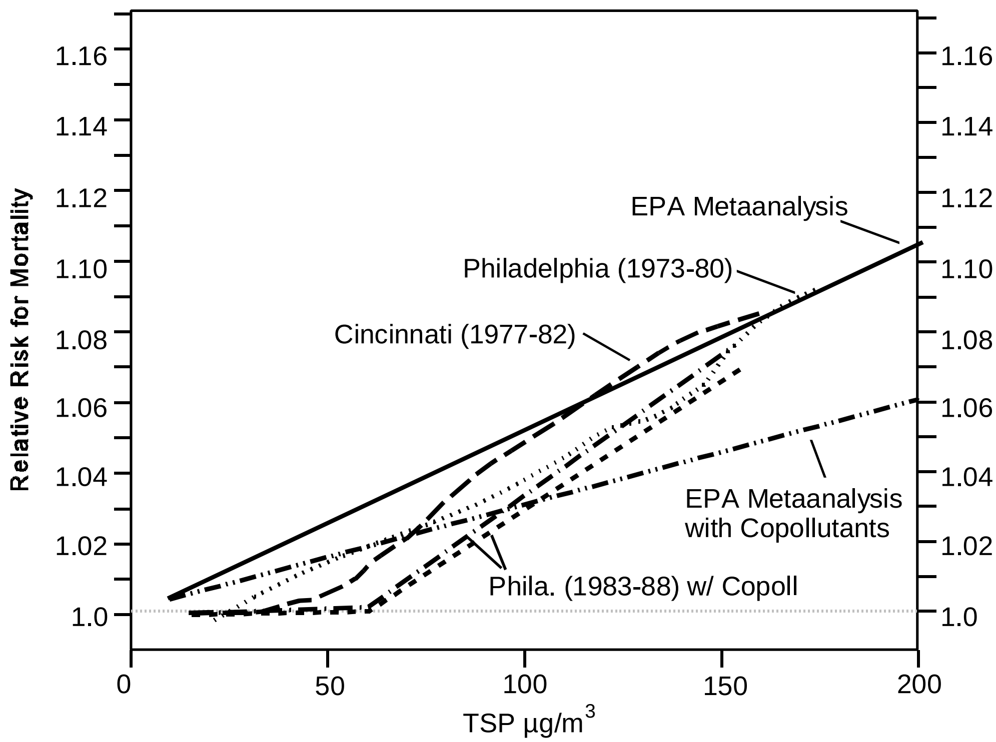

Figure F-2. Comparison of Smoothed Nonlinear and Linear Mathematical Models for Relative Risk of Total Mortality Associated with Short-Term TSP Exposure (CD, Figure 13-6). Curves show smoothed nonparametric models for Philadelphia (based on Schwartz 1994b) and for Cincinnati (based on Schwartz, 1994a), and piecewise linear models for Philadelphia (based on Cifuentes and Lave, 1996). Solid curve shows linear model from EPA metaanalysis using studies with no copollutants, dash-dot curve shows linear model from EPA metaanalysis using studies with SO_2 as a copollutant (described in CD Chapter 12).

higher cutpoint concentrations, assumptions concerning cutpoint concentrations can make a substantial difference in the estimates of risks associated with PM.

For the concentration-response relationship of mortality from long-term exposures (Table F-3E), the upper cutpoint eliminates estimated risk for Philadelphia County because Philadelphia County's annual mean concentrations are below 18 $\mu g/m^3$. For health risks both from short-term and long-term exposures, the sensitivity of estimates of risks would be expected to vary with location, especially for locations with substantially different overall PM air quality (e.g., Los Angeles County).

2. Effect on Pooled Concentration-Response Analyses Using Studies with Different Averaging Times

In their review of the PM mortality literature, the CD pointed out that heterogeneity in averaging time is an important factor to consider in assessing results (CD, p.12-72). In the PM risk analysis estimates from a number of studies have been pooled for several endpoints. For the mortality pooled analysis, studies that used averaging times ranging from 1 to 5 day mean PM concentrations have been included. Table F-4 disaggregates the pooled analysis to examine the effect of restricting the estimates of mortality risk to those studies using only the same averaging time (with the exception of the three-day and five-day mean studies, which were combined). Results vary considerably over averaging times. In the base case analysis, two-day mean air quality concentrations were used to estimate mortality, since the largest number of functions used that averaging time. Table F-4 indicates that using two-day mean concentrations to represent Philadelphia County PM_{10} concentrations results in an increase in the risk estimates predicted by the single study that reported results related to a one-day mean concentration (Kinney et al., 1995), and a slight increase in the risk predicted for the set of two studies using three- to five-day mean concentrations (Schwartz, 1993 and Pope et al., 1992). However, the Table also indicates that applying an alternative averaging time, such as one-day or five-day mean concentrations, results in no apparent difference in estimated risk from the base case two-day mean assumption.

3. Effect of Using Concentration-Response Relationships Simultaneously Considering Copollutants

PM is part of a mix of combustion source pollutants originating from a variety of stationary and mobile sources and, thus generally occurs along with other pollutants generated by combustion sources (e.g., sulfur oxides, nitrogen oxides, volatile organic compounds) or produced through the transformation of these pollutants (e.g., O_3). Such copollutants could either serve as potential confounders of the observed PM-health associations or as effect modifiers that influence the magnitude of PM associated effects. The studies used in the risk analysis provide PM coefficients from areas with widely varying levels of copollutants. One approach to controlling for the potential effects of copollutants is to include copollutants simultaneously in the model with PM when estimating the PM coefficient for a health endpoint. However, this method may be limited by collinearity in the pollutants of interest (Samet et al., 1996b). (For a fuller treatment of copollutants, potential confounding, and the significance of observed variations across study locations, see Chapter V and CD, Chapters 12 and 13).

The base case analysis used concentration-response relationships estimated without inclusion of copollutants, and it is not possible to directly estimate the sensitivity of the base case results taking into account the effect of simultaneous inclusion of copollutants, since not all the studies used for the base case examined copollutants in this manner. As an alternative, the sensitivity of individual study estimates in relationship to inclusion of copollutants is examined in Tables F-5A and F-5B. Table F-5A provides a comparison of the coefficients for studies that reported PM coefficients both with and without inclusion of copollutants, and Table F-5B provides the risk estimates obtained from applying those coefficients to Philadelphia County in the risk analysis. The results in these two tables provide a more general sense of how much of an effect inclusion of copollutants typically has on the magnitude of the health risk estimates and, thus, potentially on the base case results. The results for many, but not necessarily all, of the studies are consistent with the assessment in the CD that PM effect sizes and their statistical uncertainty in most studies showed little sensitivity to the adjustment for copollutants (CD, p.13-55).

Two substantial uncertainties remain concerning copollutants and the method of controlling for their effects through simultaneous inclusion in the health risk model. First, to what degree is it possible that the associated copollutant does not have a bona fide independent effect on mortality separate from PM? If the copollutant does not have an independent effect on mortality, then changes in the PM coefficient resulting from inclusion of the second pollutant may just be the results of collinearity between the pollutants and may not accurately reflect the underlying PM coefficient. Second, if the changes seen with inclusion of copollutants actually do reflect a bona fide improvement in the estimate of the PM effect, then is it possible simultaneous inclusion of additional copollutants would further reduce the coefficient? As pointed out by Samet et al. (1996b) and in Chapter V, examination of effects within a single location may often be limited by collinearity between pollutants and comparison across geographic areas may be required for a fuller assessment of the potential effects of copollutants on reported PM concentration-response relationships.

4. Sensitivity Analysis Concerning Reduction in the Slope of Concentration-Resposer Relationships for Risks from Long-Term Exposures

Two major concerns have been raised concerning whether the slope of the concentration-response relationships from recent studies of mortality from long-term exposures (Dockery et al., 1993, Pope et al., 1995) may be misestimated. One major uncertainty concerning the studies of health risks associated with long-term exposures to PM for adults is the potential relevance of air quality concentrations previous to the period of monitoring in the study. If long-term air quality concentrations previous to the period being monitored: 1) are relevant for a substantial portion of the population for the endpoint being studied, and 2) are substantially different than concentrations monitored during the study, then the actual long-term concentration-response relationship may be substantially different than that observed in the reported study (CD, p.13-34). The second major uncertainty relates to whether inadequate control of potential confounders may substantial alter the reported concentration-response relationships (CD, pp. 12-140-43, 12-165, 12-176-178).

The question of the degree to which previous (from years to decades) air quality exposures might have affected mortality risk is complex.[1] In addition, quantitative information

[1] Judging the extent to which previous air quality may be a significant concern for the estimates of risk from long-term exposures requires consideration of both of past air quality variability *and* of the relevant exposure period that might be expected to affect mortality risk for a substantial portion of the cohort population. The CD notes that a detailed investigation of temporal relationships has not been attempted in the cohort studies, but also notes that if

on the levels of previous air quality concentrations is difficult to ascertain, especially for $PM_{2.5}$. The CD reports that for the monitoring data reported in the Six City mortality study, downward trends in $PM_{2.5}$ mass are evident for four of the six cities (CD, p. 13-14).

Given these uncertainties in developing a quantitative basis for a sensitivity analyses concerning historical air quality, Table F-6 simply shows the potential impact of mortality risk estimates associated with long-term exposures if one assumes that previous air quality concentrations reduce the observed slope of the PM concentration-response relationship by 33% (modeling the case if relevant previous $PM_{2.5}$ concentrations averaged approximately 50% higher than that monitored in the study period) and by 50% (modeling the case if relevant previous $PM_{2.5}$ concentrations were twice as high). As expected, positing that the most important $PM_{2.5}$ concentrations in regards to effects on mortality risk occurred before the study monitoring period leads directly to similarly proportional reductions (approximately 33% and 50%) in the estimates of long-term mortality risk. To the extent that the estimates of mortality risks from long-term exposure reflect the net sum of acute events that take place over that year (which will occur when increases in daily death rates associated with acute events are not subsequently canceled by decreases (“harvesting”) (CD p.12-139), this component of mortality risk from long-term exposures risk is not sensitive to assumptions about previous air quality.

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responses reflect primarily the last few years of integrated exposure then the concurrent average monitoring data would be reasonably predictive (CD, p. 12-171, 12-181). Some findings from air pollution epidemiology suggest recent exposures may be of primary importance. The reduction in mortality incidence observed with a reduction in PM concentrations for 14 months in Utah Valley suggests that a significant amount of the mortality of substantial prematurity associated with particles in that location did not appear dependent on exposures over the span of years, since changes in mortality rates could be observed with a relatively brief temporal change (a 14 month period of reduced concentrations) in long-term average PM pollution.

Observations of the temporal relationship of exposure to mortality risk for a large portion of cardiovascular mortality (deaths from myocardial infarction) and for lung cancer from cohort studies on active cigarette smoke exposure suggest that elevated risks for myocardial infarction generally return to close to baseline nonsmoking relative risks within three to ten years (Rosenberg et al., 1985; 1990) and that much of the lung cancer risk is reduced close to the risk for never smokers (compared to the marked elevation in relative risk for lung cancer among current smokers) within 10-15 years after cessation of smoking (USEPA, 1992, Table 4-6 and 4-7). The significance of these findings to air pollution effects cannot be assumed, since quite distinct mechanisms for cigarette smoking and particular matter exposure and mortality from cardiovascular and lung cancer causes may be likely. However, the smoking cohort studies show that in one area in which the temporal relationship of exposure to mortality risk from cardiovascular and lung cancer causes has been examined, evidence suggests recent exposures may be substantially more important than less recent exposures.

Similar slope reductions can also serve to model concerns about uncontrolled confounding. The CD provides as an example how inclusion of additional ecological variables can attentuate the PM2.5-mortality relationship observed in a initially simply age- and race-adjusted dataset. The direction and extent of change in slope that might be observed by control of such confounders in a prospective cohort design, which features individual data for some risk factors is not certain (CD, pp. 12-176-77), however for the purposes of sensitivity analyses reductions in slope of 33-50% for the long-term studies will be assumed appropriate appropriate to reflect the viewpoint that exhibits substantial concerns about residual uncontrolled confounding in these studies. These would result in the same proportional reductions of approximately 33-50% in the estimates of long-term mortality risk (relative to base case assumptions) as when this slope reduction was considered as a sensitivity analysis for the potential effects of previous air quality.